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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,756	01/30/2002	Jian Zhang	PB0177	8956

7590

04/14/2004

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EXAMINER
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LY, CHEYNE D

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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**Office Action Summary**

Application No.

10/060,756

Applicant(s)

ZHANG, JIAN

Examiner

Cheyne D Ly

Art Unit

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**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --****Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 28 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above claim(s) 7,12-31,34-38 and 40-47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6,8-11,32,33,39,48 and 49 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-49 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____.   |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>1/28/04</u> .   | 6) <input type="checkbox"/> Other: _____.                                   |

### **DETAILED ACTION**

1. Applicant's arguments filed January 28, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.
2. The addition of claims 48 and 49 has been acknowledged.
3. Claims 1-6, 8-11, 32, 33, 39, 48, and 49, SEQ ID NO. 1, are examined on the merits.
4. FINAL OFFICE ACTION.

### **CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH**

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.
7. This rejection is necessitated by Applicants amendments.
8. Specific to claim 1, lines 6, 9, and 16, claims 2 and 3, line 2, and claims 48 and 49, lines 4, 7, and 13, the limitation of "complete complement" has not been found in the instant specification. Therefore, the new limitation is considered to be new matter because

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"complete complement" is different from the disclosed limitation of "complement" in the original claims. Claims 4-6, 8-11, 32, 33, and 39 are rejected for being dependent from claim 1.

#### **LACK OF UTILITY UNDER 35 U.S.C. § 101**

9. The pending claims have been reviewed in light of the Utility Examination Guidelines and Guidelines for Examination of Patent Applications under 35 U.S.C. 112, first paragraph, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1092-1111, Friday, January 5, 2001.
10. The examiner is using the following definitions in evaluating the claims for utility.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

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11. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. § 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

12. This rejection is maintained with respect to claims 1-6, 8-11, 32, 33, and 39, as recited in the previous office action mailed October 18, 2003. The instant rejection has been extended to claims 48 and 49.

13. This rejection is necessitated by Applicants amendments.

#### **RESPONSE TO ARGUMENT**

14. Applicant's pointed to support in the specification has been fully considered, however, Applicant's argument does not help Applicant overcome the instant rejection because asserted utility has not been supported by a specific and substantial utility.

15. The pointed to support of Table 1 and Figure 5 which disclose the claimed invention as "strongly expressed in testis, but at very low levels in other tissues" has been acknowledged. However, the pointed to citation does not support Applicant's assertion that the claimed invention has specific and substantial utility as potential therapeutic as well as diagnostic roles in cancer due to the pointed disclosure only compares expression between tissues without any indication of the comparison being made between normal tissues and cancerous tissues.

16. Further, the critical limitation of claims 1-6, 8-11, 32, 33, 39, 48, and 49 is the polynucleotide SEQ ID NO: 1. Applicant discloses HTPL-L cDNA is closely related to sequences known in the art via BLAST query into the GenBank database. "Globally, the human HTPL proteins resemble a putative mouse transcript...with 66% amino acid identity

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and 78% amino acid similarity over the entire open reading frame”. Further, motif (subset of the claimed sequence) searches using Pfam, PROSITE pattern, and profile databases identify several known domains shared with Patched, including the Patched domain and the Sterol sensing domain. “The presence of these domains in HTPL-L suggests that HTPL-L, like Patched and other Patched domain containing proteins, is involved in the Hedgehog signaling pathway” (page 137-139). It is acknowledged that the disclosure cited above supports that the claimed sequence resembles that of a mouse protein with these criteria 66% amino acid identity and 78% amino acid similarity over the entire open reading frame. Further, Applicant uses a subset of the claimed sequence (motif) to indirectly associate said sequence with the Hedgehog signaling pathway. However, Applicant does not provide any information, beyond indirect conclusions via sequence comparison, regarding the activity or function that supports the assertion that said claimed sequence has specific and substantial utility as potential therapeutic as well as diagnostic roles in cancer (page 4, lines 13-18).

17. It is noted that applicant has identified a sequence which is known in the prior art and which has a stated sequence similarity to the claimed sequence. Absent factual evidence, one skilled in the art would have reason to doubt that sequence similarity alone would reasonably support the assertion that the biological activity of the claimed subject matter would be the same as that of the similar sequence. Furthermore, it is unclear whether the similar sequence identified in the prior art has actually been tested for the biological activity or whether this also is an asserted biological activity based upon sequence similarity to yet a different sequence. Note that it would have been well known in the art that sequence similarity does

not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities.

18. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. The disclosure of “the premature stop of protein translation, HTPL-S contains a partial Patched domain, a complete Sterol-sensing motif and seven transmembrane domains” supports the example above. Due to the structural changes resulted from the “premature stop”, it is inclusive whether the claimed invention has the same properties as that of other Patched proteins involved in the Hedgehog signaling pathway. Therefore, the instant specification fails to conclusively support that the claimed invention has similar function as other Patched proteins involved in the Hedgehog signaling pathway.

19. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Lopez et al. (Molecular Biology, 32:881-891, 1999); Attwood (Science, 290:471-473, 2000); Gerhold et al. (BioEssays, 18(12):973-981, 1996); Wells et al. (Journal of Leukocyte Biology, 61(5):545-550, 1997); and Russell et al. (Journal of Molecular Biology, 244:332-350, 1994). However, this level of factual evidence is absent here.

### **CLAIM REJECTIONS UNDER U.S.C. § 112, FIRST PARAGRAPH**

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### **LACK OF ENABLEMENT**

21. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed sequence. For a sequence putatively assigned a biological function, even if correct, does not appear to be defined as to what use it is to be applied to. The significance of the sequence is undefined, further rendering it indiscernible how someone of skill in the art would use such an entity.

22. This rejection is maintained with respect to claims 1-6, 8-11, 32, 33, and 39, as recited in the previous office action mailed October 18, 2003. The instant rejection has been extended to claims 48 and 49.

23. This rejection is necessitated by Applicants amendments.

### **RESPONSE TO ARGUMENT**

24. Applicant is directed to the response to the Lack of Utility Rejection above.

25. The claimed invention is not supported by a specific, substantial, and credible utility or a well-established utility for the reasons set forth above (refer to 35 U.S.C. § 101 rejection), one skilled in the art would not know how to use the claimed invention.



### **LACK OF WRITTEN DESCRIPTION**

26. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

27. This rejection is maintained with respect to claims 1-6, 8-11, 32, 33, and 39, as recited in the previous office action mailed October 18, 2003. The instant rejection has been extended to claims 48 and 49.

28. This rejection is necessitated by Applicants amendments.

### **RESPONSE TO ARGUMENT**

29. Applicant's amendment which introduces the term "complete" to the limitation of complement has been acknowledged. However, the instant claims comprise subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention as discussed below.

30. The specification discloses SEQ ID NO: 1, which corresponds to DNA encoding HTPL-L. Claims 1-6, 8-11, 32, 33, 39, 48, and 49 are directed to encompass gene sequences and sequences with at least 90%, 95%, or 99% identity to the claimed sequence, and degenerate variants of the claimed sequence. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or

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she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

31. With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

*University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that: "...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that 'the inventor invented the claimed invention.'" *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

32. Therefore, only SEQ ID NO: 1 but not the full breadth of the claims 1-6, 8-11, 32, 33, 39, 48, and 49 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

**CLAIM REJECTIONS - 35 USC § 102**

33. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

34. Claims 1-6, 8-11, 48 and 49 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Carpenter et al. (1998).

35. This rejection is maintained with respect to claims 1-6 and 8-11 as recited in the previous office action mailed October 18, 2003. The instant rejection has been extended to claims 48 and 49.

36. This rejection is necessitated by Applicants amendments.

**RESPONSE TO ARGUMENT**

37. Applicant's amendment has been acknowledged. The new limitation has not been considered due to said amendment introduces the limitation of "complete complement" which has been considered to be new matter as discussed above.

38. Carpenter et al. discloses a nucleic acid that encodes multi-transmembrane protein patched (PTCH) required for germ cell development, which functions a tumor suppressor (Abstract etc.), wherein the nucleotide sequence (AF091501, 3.6 Kb) of less than 100 kb in length. The nucleotide sequence of Carpenter et al. (Position 57-61) is complementary SEQ ID NO. 1 (position 6-10) of the instant application, as in claims 1, 2, 48, and 49.

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39. Expression of PTCH and PTCH2 is detected in the testis and liver (Figure 3), as in instant claim 3.

40. A labeled nucleic probe of the AF091501 sequence which has been attached to a substrate (page 13630, cDNA cloning §), as in instant claims 4-6.

41. The AF091501 sequence has been sub-cloned into expression vector wherein it is linked to a promoter and transformed into a host cell (page 13632, Figure 2), as in instant claims 8-11.

### **CONCLUSION**

42. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

43. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

44. This application contains claims 7, 12-31, 34-38, and 40-47 drawn to an invention nonelected with traverse, filed August 04, 2003. A complete reply to the final rejection must

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include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

45. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

46. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

47. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

48. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly  
4/8/04

*Ardin H. Marschel*  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER 4/11/04